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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,369	06/25/2003	David Nathan Abraham Fox	16789 (PC25204A)	2797

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EXAMINER

ROYDS, LESLIE A

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 03/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/603,369	<b>Applicant(s)</b> FOX ET AL.	
	<b>Examiner</b> Leslie A. Royds	<b>Art Unit</b> 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 February 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,6,9,10,12 and 13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,6,9,10,12 and 13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>24 February 2006</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

**Claims 1, 6, 9-10 and 12-13 are presented for examination.**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission, supplemental Information Disclosure Statement (IDS) and revised oath/declaration, each filed February 24, 2006, have each been received and entered into the present application. Accordingly, the specification at page 6 has been amended, claims 1, 6, 10 and 12-13 are currently amended and claims 2-5, 7-8 and 11 have been cancelled.

In light of the amendments and remarks herein, the objection to the oath/declaration; the objection to the title; the objection to the specification; and the rejection of claims 1, 9-10 and 13 under 35 U.S.C. 102(b), as set forth at pages 2-7 of the previous Office Action dated August 24, 2005 have each been hereby **withdrawn**.

In view of the cancellation of claims 2-5, 7-8 and 11, the rejection of claims 2-5, 7 and 11 under 35 U.S.C. 102(b) and the rejection of claims 2-5, 7-8 and 11 under 35 U.S.C. 103(a) have each been hereby rendered **moot** as applied to such claims.

#### ***Applicant's Claim for Priority under 35 U.S.C. 119(a-d)***

Applicant's claim for the benefit of a foreign-filed application (United Kingdom Patent Application No. 0214784.1), filed June 26, 2002, under 35 U.S.C. 119(a-d) is acknowledged. Applicant is reminded that the later-filed application must be an application for patent for an

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invention that has been disclosed in the prior application (i.e., the foreign-filed application). The disclosure of the invention in the foreign application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

In light of the fact that UK Patent Application No. 0214784.1 contains sufficient support and enablement as required under 35 U.S.C. 112, first paragraph, for the presently claimed subject matter, the effective filing date of the present claims has been determined to be June 25, 2002.

***Objection to the Specification (New Ground of Objection)***

Applicant's amendments to the specification at page 6 cancelled reference to all U.S. Patents or U.S. Patent Application Publications that had been added in the amendment filed June 9, 2005 in response to the objection for the improper incorporation by reference of foreign patents or publications. However, the objection made under 35 U.S.C. 132(a) set forth at page 4 of the previous Office Action dated August 24, 2005 was made for the new incorporation of the following specific U.S. Patents into the disclosure, which are not drawn to material that was present or suggested in the specification as originally filed:

(i) U.S. Patent No. 6,743,719, drawn to a method for forming a conductive copper structure;

(ii) U.S. Patent No. 5,728,862, drawn to a method for preparing and purifying N-alkylated aspartame derivatives;

(iii) U.S. Patent No. 6,004,938, drawn to inositolglycans having insulin-like action;

(iv) U.S. Patent No. 6,232,306, drawn to derivatives of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephams;

(v) U.S. Patent No. 6,472,525, drawn to hexaazaisowurzitane derivatives and methods for producing the same;

(vi) U.S. Patent No. 6,573,279, drawn to isoquinoline derivatives or salts thereof; and

(vii) U.S. Patent No. 6,576,761, drawn to a process for the preparation of cephem compounds.

The objection under 35 U.S.C. 132(a) was not made generally against the inclusion of U.S. Patents or U.S. Patent Application Publications that were newly added. Rather, it was made specifically against those U.S. Patents cited above that are drawn to material that was not present or suggested in the specification as originally filed.

The cancellation of the reference(s) to all U.S. Patents and U.S. Patent Application Publications has rendered the specification once again subject to an objection for the improper incorporation by reference of WIPO documents and publications. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication, is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by a statement executed by the Applicant, or a practitioner representing the Applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. Please see 37 C.F.R. 1.57(f).

***Claim Rejection - 35 USC § 112, Second Paragraph (New Ground of Rejection)***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP §2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In the present instance, claim 1, for example, recites the broad limitation "for the palliative treatment of hypertension", and then goes on to state "including essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with atherosclerosis and renovascular hypertension, congestive heart failure, angina, stroke, diabetes and impaired glucose tolerance", a narrower statement of the limitation. Such a

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recitation renders the claim indefinite because it is unclear as to whether Applicant intends to claim the use of sildenafil in combination with olmesartan for the treatment of hypertension of any etiology, or if Applicant intends to claim the use of such a therapeutic combination for the specific treatment of essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with atherosclerosis and renovascular hypertension, congestive heart failure, angina, stroke, diabetes and impaired glucose tolerance. As a result, the boundaries of the claim cannot be identified.

For these reasons, claims 1, 6 and 9 fail to meet the tenor and express requirement of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

For the purposes of examination and the application of prior art, the claims will be interpreted to read upon the use of a combination therapy of sildenafil and olmesartan for the treatment of hypertension of any etiology.

### ***Claim Rejection - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

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evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6, 9-10 and 12-13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Macor et al. (U.S. Patent No. 6,087,368; 20000 in view of The Merck Manual Diagnosis and Therapy (Sixteenth Edition; 1992, p.413-431), Cecil's Textbook of Medicine (Twenty-First Edition, 2000, p.273-279 and 1279-1285), Physician's Desk Reference (55<sup>th</sup> Edition, 2001; p.323 and 330), Applicant's acknowledgement (page 7, line 31-page 8, line 2; page 8, lines 14-15, page 8, lines 22-26 and page 8, lines 31-33), Remington's Pharmaceutical Sciences (16<sup>th</sup> Edition, 1980; p.420-425), Bell et al. (U.S. Patent No. 5,250,534; 1993), Grossman (U.S. Patent No. 6,271,228; 2001), Anderson et al. (U.S. Patent Application Publication 2003/0158223; February 22, 2002) and The Merck Index (Tenth Edition, Monograph No. 8220), each already of record, for the reasons of record set forth at pages 8-15 of the previous Office Action dated August 24, 2005.

Cancellation of claims 2-5, 7-8 and 11 renders the rejection under 35 U.S.C. 103(a) moot as applied to such claims.

Applicant submits that Macor does not broadly disclose the use of any cGMP PDE5 inhibitor in combination with any angiotensin II antagonist for the treatment of cGMP-associated condition. Applicant states that Macor teaches specific compounds in combination with angiotensin II antagonists and that there is no teaching or suggestion in Macor that PDE5



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inhibitors as a class would work in combination with angiotensin II antagonists as a class and that there is no teaching or suggestion of the specific combination of sildenafil and olmesartan.

Applicant's amendments and remarks have each been considered in their entirety, but fail to be persuasive in establishing error in the propriety of the present rejection.

First, it is noted that Macor et al. was not relied upon to expressly anticipate the combination of sildenafil and olmesartan, as is now presently claimed. However, in light of the state of the art at the time of the invention, such a combination would have been *prima facie* obvious to one of ordinary skill in the art in view of the disclosure of Macor et al.

In particular, it is noted that while Macor et al. discloses particular cGMP PDE5 inhibitor compounds, such as those of the chemical structure described at col.1, line 65-col.3, line 3, the reference raises the reasonable expectation of success that a cGMP PDE5 inhibitor other than those expressly claimed by the reference would also have had, at minimum, substantially similar efficacy in treating those cGMP-associated conditions specifically disclosed by the reference. Since Macor et al. teaches that such conditions are amenable to treatment with a cGMP PDE5 inhibitor, such would have been sufficient motivation to one of ordinary skill in the art to use another known cGMP PDE5 inhibitor compound for the treatment of the same conditions with the reasonable expectation that such a compound would have achieved the same or substantially similar efficacy as those cGMP PDE5 compounds taught by Macor et al., absent factual evidence to the contrary.

Furthermore, Macor et al. discloses that such cGMP PDE5 compounds could be combined with other known agents that are also known to have efficacy in the treatment of those same cGMP-associated conditions, of which the angiotensin II antagonists losartan, irbesartan,

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valsartan and candesartan are expressly disclosed. Such disclosure by Macor et al. articulates the concept that a cGMP PDE5 inhibitor compound combined with an angiotensin II antagonist could be employed for the reasonably successful treatment of the disclosed cGMP-associated conditions, which either directly overlap or render obvious the diseases presently claimed (see Office Action dated March 7, 2005 at pages 12-14 and 16-17). Once again, Macor et al. has raised the reasonable expectation of success that the combination of such a cGMP PDE5 inhibitor combined with an angiotensin II antagonist would have had efficacy in the treatment of those cGMP associated conditions disclosed by the reference. Thus, Macor et al. clearly contemplates the use of a cGMP PDE5 inhibitor in combination with an angiotensin II antagonist for the treatment of those cGMP associated conditions disclosed in the reference.

Though it is noted that Macor et al. does not expressly disclose the particular combination of sildenafil in combination with olmesartan as is now presently claimed, the absence of the disclosure of this specific combination does not negate the broader disclosure of the reference as a whole. It has already been made of record that sildenafil was a known cGMP PDE5 inhibitor and olmesartan was a known angiotensin II antagonist. Absent factual evidence to the contrary, the disclosure of Macor et al. teaching the combination of a cGMP PDE5 inhibitor with an angiotensin II antagonist would have rendered such a combination *prima facie* obvious to one of ordinary skill in the art at the time of the invention because sildenafil would have been reasonably expected to exert the same cGMP PDE5 inhibiting effect as those cGMP PDE5 inhibitors expressly disclosed by the reference and olmesartan would have been reasonably expected to exert the same antagonistic effect on angiotensin II receptors. Thus, the

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combination would also have been reasonably expected to achieve the same, or substantially similar, efficacy to the combinations expressly disclosed by Macor et al.

For these reasons and those already made of record, rejection of claims 1, 6, 9-10 and 12-13 remains proper and is **maintained**.

***Claim Rejection - 35 USC § 103 (New Ground of Rejection)***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6, 9-10 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fryburg et al. (WO 02/13798; February 2002) in view of Anderson et al. (U.S. Patent Application Publication No. 2003/0158223; February 22, 2002), Ball et al. ("Relative Efficacy of an Angiotensin II Antagonist Compared with Other Antihypertensive Agents: Olmesartan

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Medoxomil versus Antihypertensives”, *Journal of Hypertension Supplement*, 2001) and Remington's Pharmaceutical Sciences (Sixteenth Edition, 1980; p. 420-425).

Fryburg et al. teaches a method for treating patients with insulin resistance syndrome (page 6, lines 30-32), wherein the patient has the concomitant existence of two or more of hypertension (see present claims 1, 9 and 13), type 2 diabetes mellitus, impaired glucose tolerance or atherosclerosis (page 6, line 33-page 7, line 3; see present claim 1), comprising treating the patient with an effective amount of a selective cGMP PDE5 inhibitor or pharmaceutical composition thereof (page 6, lines 30-33), wherein the cGMP PDE5 inhibitor is preferably sildenafil (page 11, lines 17-21; see present claim 1, 10 and 12-13) or a pharmaceutically acceptable salt thereof (page 12, line 26), such as sildenafil citrate (page 14, lines 15-16; see present claim 6), and wherein the cGMP PDE5 inhibitor may be administered in combination (page 27, lines 13-16) with an angiotensin receptor antagonist, such as losartan (page 29, line 21; see present claim 1, 10 and 12-13). Fryburg et al. further teaches that the cGMP PDE5 inhibitor compounds may be combined with a suitable pharmaceutical excipient, diluent or carrier and formulated into tablets, capsules, multi-particulate, gels, films, ovules, elixirs, solutions or suspensions (page 20, lines 18-31; see present claims 10 and 12), and wherein an additional pharmaceutically active agent, (i.e., an angiotensin receptor antagonist) is also present (page 46, lines 1-12; see present claim 10) and also wherein the combination treatment is in the form of a kit (page 46, lines 14-15; see present claim 12).

The differences between the Fryburg et al. reference and the presently claimed subject matter lie in that the reference fails to teach:

(i) the use of olmesartan, olmesartan medoxomil or pharmaceutically acceptable salts thereof (see present claims 1, 10 and 12-13);

(ii) a kit comprising sildenafil and olmesartan or olmesartan medoxomil or salts thereof and a container (see present claim 12); or

(iii) the administration of sildenafil and olmesartan or olmesartan medoxomil or salts thereof separately, simultaneously or sequentially (see present claim 13).

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

(i) Though Fryburg et al. does not expressly teach the use of olmesartan, olmesartan medoxomil or salts thereof as the angiotensin receptor antagonist, such compounds were well known in the art at the time of the invention as having antagonistic activity on angiotensin receptors and, thus, the use of such a compound as the angiotensin receptor antagonist in combination with the disclosed cGMP PDE5 inhibitor would have been *prima facie* obvious to the skilled artisan.

In this regard, Anderson et al. (U.S. Patent Application Publication No. 2003/0158223; February 22, 2002) is cited to show that olmesartan was a known angiotensin II antagonist used for the treatment of elevated blood pressure (page 1, paragraph [0003]). Ball et al. ("Relative Efficacy of an Angiotensin II Antagonist Compared with Other Antihypertensive Agents: Olmesartan Medoxomil versus Antihypertensives", *Journal of Hypertension Supplement*, 2001) is also cited to show that olmesartan medoxomil was a known angiotensin II antagonist

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compound that proved to be more effective than losartan in reducing blood pressure in the hypertensive population (see cited abstract).

In light of such teachings, it would have been *prima facie* obvious to one of ordinary skill in the art to employ olmesartan or olmesartan medoxomil as the active angiotensin II antagonist component of the combination cGMP PDE5 inhibitor-angiotensin II antagonist therapy disclosed by Fryburg et al. Such a person would have been motivated to do so because each of olmesartan or olmesartan medoxomil was known to have the same antagonistic effect on angiotensin receptors and, therefore, would have been reasonably expected to exert the same or substantially similar efficacy in blocking such receptors as those angiotensin receptor antagonists (i.e., losartan) expressly disclosed by Fryburg et al. In fact, the teachings of Ball et al. support the conclusion that olmesartan or olmesartan medoxomil would have the same, if not enhanced, efficacy as the losartan expressly taught by Fryburg et al., since a comparative study between the two compounds demonstrated that olmesartan medoxomil was more effective than losartan at reducing blood pressure.

In addition, the use of pharmaceutically acceptable salts of olmesartan would have been a matter well within the purview of the skilled artisan. As taught by Remington's Pharmaceutical Sciences, drugs may be formulated into salts to modify the duration of action of a drug; to modify the transportation and distribution of the drug in the body; to reduce toxicity; and to overcome difficulties encountered in pharmaceutical formulation procedures or in the dosage form itself (see column 2 of page 424, first paragraph). Thus, it would have been obvious to the skilled artisan motivated by any one or more of these factors to formulate the active agent olmesartan into a pharmaceutically acceptable salt to enhance the pharmacokinetic parameters of

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the drug or to reduce the toxicity with the reasonable expectation that the therapeutic benefit of the agent in salt form would have been the same or substantially similar to that of the agent itself.

(ii) With regard to the kit of present claim 12, wherein the kit comprises sildenafil as a pharmaceutical composition and olmesartan as a pharmaceutical composition and a container to hold the compositions, the mere placement of two discrete dosage forms into a container would have been within the general knowledge of one of ordinary skill in the art at the time of the invention and, thus, would have been *prima facie* obvious. Such a person would have been motivated to do so to facilitate manufacture and dissemination of the formulations to patients in need thereof and to facilitate patient compliance with a prescribed regimen by providing such a formulation in a portable container that can be easily transported on one's person and carried to allow for convenient dosing, as necessary.

(iii) The determination of the optimum dosing regimen (i.e., that sildenafil and olmesartan are administered separately, simultaneously or sequentially) to treat hypertension with the presently claimed active agents would have been a matter well within the purview of one of ordinary skill in the art. Such a determination would have been made in accordance with a variety of factors, such as the dosage amount to be administered, the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the dosing regimen that would have actually been employed would have varied widely and, in the absence of

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evidence to the contrary, the currently claimed regimens are not seen to be inconsistent with those that would have been determined by the skilled artisan.

***Conclusion***

Rejection of claims 1, 6, 9-10 and 12-13 is deemed proper and is **maintained**.

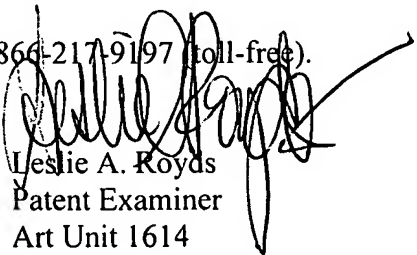
No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (8:30 AM-5:00 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
CHRISTOPHER S. F. LOW  
SUPERVISORY PATENT EXAMINER  
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Leslie A. Royds  
Patent Examiner  
Art Unit 1614

March 9, 2006